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09/767,680	01/24/2001	Asger Geppel	54337.000010	4425

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EXAMINER

KERR, KATHLEEN M

ART UNIT

PAPER NUMBER

1652

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)
	09/767,680	GEPPEL ET AL.
	Examiner	Art Unit
	Kathleen M Kerr	1652

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) Responsive to communication(s) filed on 11 October 2002.

2a) This action is FINAL. 2b) This action is non-final.

3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4) Claim(s) 1-33 is/are pending in the application.

4a) Of the above claim(s) 18-33 is/are withdrawn from consideration.

5) Claim(s) _____ is/are allowed.

6) Claim(s) 1-17 is/are rejected.

7) Claim(s) _____ is/are objected to.

8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9) The specification is objected to by the Examiner.

10) The drawing(s) filed on _____ is/are: a) accepted or b) objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) The proposed drawing correction filed on _____ is: a) approved b) disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.

12) The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) All b) Some * c) None of:
1. Certified copies of the priority documents have been received.
2. Certified copies of the priority documents have been received in Application No. _____.
3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.

14) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
a) The translation of the foreign language provisional application has been received.

15) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)	4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____ .
2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)	5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)
3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) <u>5,6,7</u> .	6) <input type="checkbox"/> Other:

DETAILED ACTION

Application Status

1. In response to the previous Office action, a written restriction requirement (Paper No. 8, mailed on September 23, 2002), Applicants filed an election received on October 11, 2002 (Paper No. 9). Claims 1-33 are pending in the instant Office action.

Election

2. Applicants' election with traverse of Group I, Claims 1-17, in Paper No. 9 is acknowledged. The traversal is on the ground(s) that the cells of Group I are related to the methods of Groups II, III, and IV and that the holding that these Groups are distinct is improper. This is not found persuasive because while the Groups are related, they are distinct for the reasons previously cite. Applicants also argue that the designated groups have not necessarily acquired a separate status in the art for examination purposes. This is not the case based on the distinct class/subclass classifications as previously cited. While the art may overlap in different class/subclass classifications, they all must be searched over the course of a complete search of the art. Searching more than one class/subclass is considered undue.

The requirement is still deemed proper and is therefore made FINAL. Claims 1-33 are pending. Claims 18-33 are withdrawn from consideration as non-elected inventions. Claims 1-17 will be examined herein.

Priority

3. The instant application is granted the benefit of priority as the continuation of PCT/DK01/00036 filed on January 18, 2001 and as a continuation-in-art of U.S. non-provisional Application No. 09/488,644 filed on January 21, 2000 as requested in the declaration and the first lines of the specification. The Examiner notes that the disclosure related specifically to cytochrome d (Claim 5) does not have support back to January 21, 2000, while all other claims examined herein (Claims 1-4 and 6-17) do.

Information Disclosure Statement

4. The information disclosure statements filed on June 19, 2001 (Paper No. 5), August 20, 2001 (Paper No. 6), and November 8, 2001 (Paper No. 7) have been reviewed, and their references have been considered as shown by the Examiner's initials next to each citation on the attached copy. On Paper No. 6, page 2, the Examiner crossed out the English abstract of JP 04036180A since it was initialed in Paper No. 7 (duplicate). Also on Paper No. 6, page 3, the Examiner considered the search report noted, but crossed out the reference since it is not printed on the face of the file. Other citation corrections were made on Paper No. 6. No action is required by Applicants.

Objections to the Specification

5. The specification is objected to for lacking updated continuity data in the first paragraph. The benefit of U.S. non-Provisional Application No. 09//488,644 in the first paragraph of the specification must be updated since said application is now abandoned. Appropriate amendment to the specification is required (see M.P.E.P. § 201.11).

6. The specification is objected to for not labeling the description of the drawings as follows: ---Brief Description of the Drawings--- on page 16. Appropriate correction is required.

7. In the specification, the Abstract is objected to for not completely describing the disclosed subject matter (see M.P.E.P. § 608.01(b)). It is noted that in many databases and in foreign countries, the Abstract is crucial in defining the disclosed subject matter, thus, its completeness is essential. The Examiner suggests the inclusion of the particular species of lactic acid bacteria disclosed (see Claim 6) as well as the particular nature of NADH oxidase, lactate dehydrogenase, and cytochrome d disclosed for completeness.

Claim Objections

8. Claim 5 is objected to for having improper form; the final period is missing. Appropriate correction is required.

9. Claim 13 is objected to under 37 C.F.R. § 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. The added requirement of being a starter culture composition does not add further limitation to the originally claimed culture in Claim 1.

Claim Rejections - 35 U.S.C. § 112

The following is a quotation of the second paragraph of 35 U.S.C. § 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

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10. Claims 1-17 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The term “culturally modified” is unclear. The specification describes lactic acid bacteria that have been treated with porphyrin in culture and, when placed in a porphyrin-free culture, retain particular characteristics induced by the porphyrin exposure. The specification describes the invention as not involving genetic engineering or classical mutagenesis (see page 4); however, the only way to maintain the porphyrin-induced characteristics in the absence of porphyrin is by some form of genetic mutation. Thus, a form of genetic engineering is practiced albeit in a very crude form. Moreover, the term “derived” also indicates some sort of genetic modification with respect to the parent cell. The Examiner suggests rewording the claim so that it is drawn to a lactic acid bacteria culture previously treated in culture with a particular porphyrin concentration, then removed from the porphyrin culture and placed in a different culture wherein the bacteria have certain characteristics. Clarification and/or amendment are required.

11. Claims 3-5 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The term “detectable amount” is unclear without recitation of a detection method. Methods of enzyme/protein detection range in sensitive from protein recognition to mass spectrometry analysis, all of which “detect” varying thresholds of cytochrome d that are present. Without definition of the detection methods, the required limitation of an amount of cytochrome is unclear. Clarification is required.

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12. Claims 7 and 17 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The term “including” renders the claims indefinite because it is unclear whether the limitations following the phrase are part of the claimed invention. See M.P.E.P. § 2173.05(d). Clarification is required.

13. Claims 8 and 9 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In Claim 8, the term “about”, in reference to a temperature, indicates a breadth of temperature that is unclear. Does this adjective mean +/-5 degrees? 10 degrees? The meaning is unclear. Appropriate clarification is required.

14. Claims 10-12 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The abbreviations “NOX” and “LDH” are unclear without definition upon their first appearance in the claims. Appropriate clarification is required. The Examiner suggests these terms be replaced with “NADH oxidase (NOX)” and “lactate dehydrogenase (LDH)” for clarity.

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

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15. Claims 1-17 are rejected under 35 U.S.C. § 112, first paragraph, written description, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claim 1 is drawn to lactic acid bacteria that are claimed solely by function and without any structural limitations. Claim 7 is included in the instant rejection because the language does not limit the claim to DSM 12015 as noted above in the rejection under 35 U.S.C. § 112, second paragraph.

The Court of Appeals for the Federal Circuit has recently held that a “written description of an invention involving a chemical genus, like a description of a chemical species, ‘requires a precise definition, such as be structure, formula [or] chemical name,’ of the claimed subject matter sufficient to distinguish it from other materials.” University of California v. Eli Lilly and Co., 1997 U.S. App. LEXIS 18221, at *23, quoting Fiers v. Revel, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) (bracketed material in original). To fully describe a genus of genetic material, which is a chemical compound, applicants must (1) fully describe at least one species of the claimed genus sufficient to represent said genus whereby a skilled artisan, in view of the prior art, could predict the structure of other species encompassed by the claimed genus and (2) identify the common characteristics of the claimed molecules, e.g., structure, physical and/or chemical characteristics, functional characteristics when coupled with a known or disclosed correlation between function and structure, or a combination of these.

In the instant specification, lactic acid bacteria (specifically *L. lactis* subsp. *lactis*) treated in culture with porphyrin (specifically, haemin) are described. These bacteria have been affected in their NOX and LDH activity as well as their cytochrome d content that alters their oxygen

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consumption even after the bacteria are placed in a different, porphyrin-free culture. As noted above, a specific genetic alteration to explain this effect is likely, but not described (i.e., no structure of the claimed bacteria is described). The instant specification describes a single species of the claimed genus without any common structural characteristics being described so that one of skill in the art could ascertain the structure of other members of the genus. For these reasons, the full scope of the claimed invention lacks adequate written description.

16. Claim 7 is rejected under 35 U.S.C. § 112, first paragraph, enabling deposit, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. To practice the instant methods, one of skill in the art is required to have DSM 12015. While the instant specification contains deposit information on page 18 and added to the end of the specification, the requirements to enable such a deposit have not been fully met by the instant application. To enable the instant claims by enabling the deposit of DSM 12015, the record must also contain a statement certifying that all restrictions on accessibility to said deposit be irrevocably removed by Applicant upon the granting of the patent (see M.P.E.P. § 2404.01); this statement may be certified by Applicants or Applicants' representative.

Claim Rejections - 35 U.S.C. § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

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17. Claims 1, 6, 7, 10, 11, 13, 14, 15, and 17 are rejected under 35 U.S.C. § 102(b) as being anticipated by Kaneko *et al.* (see IDS Paper No. 6). The instant claims are drawn to *Lactococcus lactis* cells that have increased porphyrin content, decreased NOX by at least 10%, and are in liquid form with a bacterial nutrient having 10^4 to 10^{12} CFU/g.

Kaneko *et al.* teach *Lactococcus lactis* subsp. *lactis* 3022 cells grown in 6.5 mg/L hemin ($= 10 \mu\text{M}$), a porphyrin compound (see page 2644, right column). Said cells have 75% the NOX activity of those not treated with hemin (see Table 3 on page 1648). The culture is liquid and contains bacterial nutrients; the dry weight of the cells (2.27 mg/ml) inherently falls within the CFU range claimed as a starter culture.

18. Claims 2-5, 8, 9, and 12 are rejected under 35 U.S.C. § 102(b) as being anticipated by Kaneko *et al.* (see IDS Paper No. 6) as evidenced by Geppel *et al.* (WO 01/52668). The instant claims are drawn to *Lactococcus lactis* cells that have increased porphyrin content to at least 0.1 ppm, having cytochrome d at 0.1 ppm, having increased oxygen consumption under particular conditions (see Claims 8-9), and having decreased LDH activity by at least 10%.

Kaneko *et al.* teach *Lactococcus lactis* subsp. *lactis* 3022 cells grown aerobically in 6.5 mg/L hemin ($= 10 \mu\text{M}$), a porphyrin compound (see page 2644, right column). Geppel *et al.* teach a different strain of *Lactococcus lactis* subsp. *lactis* treated with 10 mg/L haemin (see page 18) and evidences many of the characteristics inherent in the cells taught by Kaneko *et al.*

While Kaneko *et al.* do not teach that their cells have at least 0.1 ppm porphyrin, this feature is inherent by virtue of the treatment of the cells, which treatment is the same as found in Geppel *et al.* Table 4 on page 25 of Geppel *et al.* evidences that haemin, a porphyrin compound,

is inherently present in the cells of Kaneko *et al.* to the concentrations required by the instant claims.

While Kaneko *et al.* do not teach that their cells have at least 0.1 ppm of cytochrome d, this feature is inherent by virtue of the treatment of the cells, which treatment is the same as found in Geppel *et al.* Figure 7 in Geppel *et al.* evidences that cytochrome d is inherently present in the cells of Kaneko *et al.* and on page 28 of Geppel *et al.*, the amount of cytochrome d is noted as 13 ppm that exceeds the concentrations required by the instant claims.

While Kaneko *et al.* do not teach that their cells have increased oxygen consumption, this feature is inherent by virtue of the treatment of the cells, which treatment is the same as found in Geppel *et al.* Table 3 in Geppel *et al.* evidences that 69% of the initial oxygen is inherently consumed after 2 hours in the cells of Kaneko *et al.*

While Kaneko *et al.* do not teach that their cells have decreased LDH activity, this feature is inherent by virtue of the treatment of the cells, which treatment is the same as found in Geppel *et al.* Table 2 in Geppel *et al.* evidences that a 15-20% decreased in LDH activity inherently accompanies haemin treatment under aerobic conditions (compare Fermentations C and D) 69% in the cells of Kaneko *et al.*

The Examiner notes that Geppel *et al.* (WO 01/52668) is the publication of the instant application from the international filing and does not pre-date the effective filing of the instant claims. Geppel *et al.* is used in this rejection to “show that a characteristic not disclosed in the reference is inherent” (see M.P.E.P. § 2131.01); such evidence is permissible in a 102-type rejection. Additionally, “the critical date of extrinsic evidence showing a universal fact need not antedate the filing date” (see M.P.E.P. § 2131.01).

Conclusion

19. Claims 1-17 are not allowed for the reasons identified in the numbered sections of this Office action. Applicants must respond to the objections/rejections in each of the numbered sections in this Office action to be fully responsive in prosecution.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kathleen M Kerr whose telephone number is (703) 305-1229. The examiner can normally be reached on Monday through Friday, from 8:30am to 5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathupura Achutamurthy can be reached on (703) 308-3804. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 872-9306 for regular communications and (703) 872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

KMK
December 27, 2002

